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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/475,822	06/07/1995	MARC ALIZON	3495.0010-24	4214

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/475,822	ALIZON ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2005* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47,51 and 52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47,51 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3/9/05
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.129(a)

1. This application is subject to the provisions of Public Law 103-465, effective June 8, 1995. Accordingly, since this application has been pending for at least two years as of June 8, 1995, taking into account any reference to an earlier filed application under 35 U.S.C. 120, 121 or 365(c), applicant, under 37 CFR 1.129(a), is entitled to have a first submission entered and considered on the merits if, prior to abandonment, the submission and the fee set forth in 37 CFR 1.17(r) are filed prior to the filing of an appeal brief under 37 CFR 1.192. Upon the timely filing of a first submission and the appropriate fee under 37 CFR 1.17(r), the finality of the previous Office action is withdrawn. In view of 35 U.S.C. 132, no amendment considered as a result of payment of the fee set forth in 37 CFR 1.17(r) may introduce new matter into the disclosure of the application.

Claim Rejections - 35 USC § 112 – Written Description

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 47, 51 and 52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

Claims 47, 51 and 52 are generic claims which are based upon a single species. That is, Applicant identified a single HIV-1 sequence. However, the claims encompass a genus of any HIV-1 nucleic acid anywhere, which genus comprises each of the hundreds of millions of different variants which exist around the world. These HIV-1 variants are not disclosed in the specification resulting in a genus which includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only a single HIV-1 sequence. Thus, applicant has express possession of only a single HIV-1 sequence in a genus which comprises hundreds of millions of different possibilities.

The claim indicates no common element or attributes of the sequences that is required. No structural domains such as specific amino acid sequences, or functional domains or any common attribute whatsoever is required. Simply a virus which shares the same name as that identified by Applicant (and regarding which Applicant lost an interference to Chang et al regarding priority). Claims 47, 51 and 52 have no structural

limitations or requirements which provide guidance on the identification of sequences which even distinguish, in a structural way, HIV-1 from any other similar lentivirus such as SIV. Claims 47, 51 and 52 provide no written description of alleles, of insertions, of deletions or of any other variation in the HIV-1 sequence.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the sequence a an HIV-1 sequence, without any specific structure given in claims 47, 51 and 52, is precisely the situation of naming a type of material which is generally known to likely exist, but except for the single specific example of a particular HIV-1 sequence provided in the specification, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as an HIV-1 sequence, without any definition of the particular sequences claimed. Claims 47, 51 and 52 envision a scope which encompasses any HIV-1 sequence but the specification does not provided the detailed chemical structure of any DNA other than the single HIV-1 sequence described.

In the instant application, a single specific sequence is described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than the single sequence expressly disclosed. Therefore, claim 47 fails to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 112 – Enablement

4. Claims 47, 51 and 52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detection of the specific HIV-1 sequence disclosed in the specification, does not reasonably provide enablement for detection of

HIV-1 variants which are not disclosed in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a methods of detecting the presence of HIV-1 in a subject comprising the steps of detecting HIV-1 nucleic acids present in the supernatant of a biological sample. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims encompass diagnosis of any HIV-1 virus, whether there is significant shared sequence or not. The claim includes no structural elements whatsoever regarding the Human Immunodeficiency virus. No specific polymorphisms in HIV-1 or sequence alterations are identified. The claims encompass any insertion, any deletion, any substitution or any alteration whatsoever relative to the HIV-1 sequence disclosed

in the specification. No specific sequences are recited for the HIV-1 sequences are provided so these claim terms broadly encompass any sequence which can be so named.

Quantity of Experimenation

The quantity of experimentation in this area is extremely large since determination of the diagnostic efficacy of any particular HIV-1 sequence with relation to the presence of the virus would require identification of a disease cohort, since different individuals are infected with different subtypes of the HIV-1 virus and different probes would function to detect different subtypes or other variants. In the case of HIV-1 polymorphisms, deletions, insertions and other sequence alterations, analysis of the entire cohort for the alteration would be required and performance of this method on a large enough sample to be statistically significant. This would require significant inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The prior art shows that a probe which detects one strain of HIV-1 may fail to detect other HIV-1 strains. Candotti et al (AIDS (1991) 5(8):1003-7) notes "Moreover, the DNA amplified from two other isolates did not hybridize with the corresponding probe despite efficient PCR. Base substitutions were detected in the regions of proviral genomes involved in oligonucleotide annealing and were assumed to be responsible for the **failure** of both amplification and probing. Our data confirm that the genetic variability of HIV-1 may reduce the efficiency of PCR as a diagnostic procedure,

especially in the case of African isolates (emphasis added)." So even 8 years after the filing date of the specification from which priority is claimed, there was significant variability in the detection of HIV-1 using HIV-1 nucleic acids. This unpredictability is heightened with regard to the current application which was written in a time when oligonucleotide synthesis was uncertain and difficult, the PCR method used by Candotti had not yet been invented, and probe synthesis, selection and detection methods were significantly more primitive than they were in 1991, much less now in 2004.

Working Examples

The specification has one working example of an HIV-1 sequence. There are no other working examples.

Guidance in the Specification.

The specification, while providing a general review of methods to diagnose HIV-1 does not provide teachings sufficient to overcome doubts raised in the art with regards to the unpredictability of probes to function and with regard to the absence of any sequence for any HIV-1 other than the single sequence disclosed. It would essentially be a trial and error process to make and use the many possible diverse species of HIV-1 encompassed by the claims in order to diagnose disease.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the art is high as shown by the cited prior art, the specification provides one with little description

or guidance that leads one to a reliable method of diagnosis of HIV-1. One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Further the specification does not provide guidance to overcome art recognized problems in diagnosis required to actually use the diagnostic methods as broadly claimed for all HIV-1 nucleic acids whatever their sequence. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the small number of working examples and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Double Patenting

5. Claims 51 and 52 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,627,395 Although the conflicting claims are not identical, they are not patentably distinct from each other because the issued claims represent a species which anticipates the current generic claims.

Claims 1-6 of U.S. Patent No. 6,627,395 teach a method for preparing and detecting HIV-1 RNA from a lysate of an HIV-1 virus, said method comprising: (a) providing a biological sample that comprises human CD4+ lymphocytes infected with HIV-1 virus; (b) separating said virus from said human CD4+ lymphocytes; (c) centrifuging said separated virus to form a fraction comprising concentrated virus; (d)

isolating said fraction comprising concentrated virus; (e) lysing said virus; (f) precipitating the RNA of said virus; and (g) detecting said viral RNA.

2. The method of claim 1, wherein said method comprises banding said virus on a sucrose gradient or a metrizamide gradient.

3. The method of claim 1, wherein said method comprises pelleting said virus.

4. The method of claim 3, wherein said method comprises precipitating said virus with polyethylene glycol.

5. The method of claim 1, wherein the virus is lysed with SDS.

6. The method of claim 1, wherein said nucleic acid is precipitated with trichloroacetic acid.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Response to Arguments

7. Applicant's arguments filed March 9, 2005 have been fully considered but they are not persuasive.

Applicant simply argues that the claims are allowable. The rejections above contravert that position.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
4/12/05